

1. An isolated DNA molecule comprising a nucleotide sequence coding for Alzheimer Related Membrane Protein (ARMP) or a functional fragment or variant of the protein.
2. The DNA molecule of claim 1 wherein the nucleotide sequence codes for the amino acid Sequence ID No:2.
3. The DNA molecule of claim 1 wherein the nucleotide sequence codes for the amino acid Sequence ID No:133.
4. The DNA molecule of claim 1 wherein the nucleotide sequence codes for the amino acid Sequence ID No:134.
5. The DNA molecule of claim 1 wherein the nucleotide sequence codes for human ARMP and is selected from the group consisting of
  - (a) Sequence ID No:1;
  - (b) nucleotides 186 to 2764 of Sequence ID No:1;
  - (c) Sequence ID No:5;
  - (d) Sequence ID No:132; and
  - (e) nucleotides 1 to 1017 and 1117 to 2791 of sequence ID No:1.
6. The DNA molecule of claim 1 wherein the nucleotide sequence codes for mouse ARMP and has nucleotide Sequence ID No:134.
7. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of
  - (a) a deoxyribonucleotide sequence complementary to Sequence ID No:1;

- (b) a ribonucleotide sequence complementary to Sequence ID No:1;
- (c) a ribonucleotide sequence complementary to the deoxyribonucleotide sequence of (a) or to the ribonucleotide sequence of (b);
- (d) a nucleotide sequence of at least 12 consecutive nucleotides capable of hybridising to Sequence ID No:1; and
- (e) a nucleotide sequence capable of hybridising to a nucleotide sequence of (d).

8. The DNA molecule of claim 1 wherein the nucleotide sequence is the ARMP-coding nucleotide sequence of ATCC Deposit No. \_\_\_\_\_.

9. An isolated DNA molecule comprising a nucleotide sequence selected from the group consisting of

- (a) Sequence ID No:3;
- (b) Sequence ID Nos:6 to 125;
- (c) Sequence ID Nos:126 to 131;
- (d) Sequence ID Nos:138 to 148; and
- (e) Sequence ID Nos:149 to 159.

10. An isolated DNA molecule comprising a nucleotide sequence coding for E5-1 protein or a functional fragment or variant of the protein.

11. The DNA molecule of claim 10 wherein the nucleotide sequence is selected from the group consisting of:

- (a) a nucleotide sequence coding for amino acid Sequence ID No: 137; and
- (b) nucleotide Sequence ID No: 136.

12. The DNA molecule of claim 10 wherein the nucleotide sequence is the E5-1 coding nucleotide sequence of ATCC Deposit No. \_\_\_\_\_.

13. A ~~isolated~~ nucleic acid molecule comprising a ~~nucleotide~~ sequence selected from the group consisting of

- (a) a deoxyribonucleotide sequence complementary to Sequence ID No:134;
- (b) a ribonucleotide sequence complementary to Sequence ID No:134;
- (c) a ribonucleotide sequence complementary to the deoxyribonucleotide sequence of (a) or to the ribonucleotide sequence of (b);
- (d) a nucleotide sequence of at least 12 consecutive nucleotides capable of hybridising to Sequence ID No:134; and
- (e) a nucleotide sequence capable of hybridising to a nucleotide sequence of (d).

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14. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of

- (a) a deoxyribonucleotide sequence complementary to Sequence ID No:136;
- (b) a ribonucleotide sequence complementary to Sequence ID No:136;
- (c) a ribonucleotide sequence complementary to the deoxyribonucleotide sequence of (a) or to the ribonucleotide sequence of (b);
- (d) a nucleotide sequence of at least 12 consecutive nucleotides capable of hybridising to Sequence ID No:136; and
- (e) a nucleotide sequence capable of hybridising to a nucleotide sequence of (d).

15. An isolated DNA molecule comprising a nucleotide sequence coding for a mutant form of Alzheimer Related Membrane Protein.

16. The A molecule of claim 15 wherein the nucleotide sequence has at least one mutation selected from the group consisting of

- i) 685, A→C      ii) 737, A→G      iii) 986, C→A
- iv) 1105, C→G      v) 1478, G→A      vi) 1027, C→T
- vii) 1102, C→T and viii) 1422, C→G.

17. The DNA molecule of claim 15 wherein the nucleotide sequence comprises the nucleotide Sequence ID No:1 or 132 having at least one mutation selected from the group consisting of

- i) 685, A→C      ii) 737, A→G      iii) 986, C→A
- iv) 1105, C→G      v) 1478, G→A      vi) 1027, C→T
- vii) 1102, C→T and viii) 1422, C→G.

18. A recombinant vector comprising the DNA molecule of any of claims 1 to 17.

19. A host cell transfected with a recombinant vector comprising the DNA molecule of any of claims 1 to 17.

20. Purified Alzheimer Related Membrane Protein or a functional fragment or variant thereof.

21. The protein of claim 20 comprising an amino acid sequence selected from the group consisting of

- (a) Sequence ID No:2;
- (b) Sequence ID NO:4;
- (c) Sequence ID No:133; and
- (d) Sequence ID No:135.

22. Substantially pure mutant Alzheimer Related Membrane Protein.

23. The protein of claim 22 having a mutation selected from the group consisting of

- i) M 146L; ii) H 163R; iii) A 246E;
- iv) L 286V; v) C 410Y; vi) A 260V;
- vii) A 285V; and viii) L 392V.

24. Substantially pure E5-1 protein.

25. The protein of claim 25 comprising the amino acid Sequence ID No:137.

26. An isolated DNA molecule comprising a splice variant of the nucleotide Sequence ID No:1.

27. The DNA molecule of claim 26 comprising nucleotides 1 to 1017 and 1117 to 2791 of Sequence ID No:1.

28. A nucleotide sequence which codes for an antigenic determinant of a protein selected from the group consisting of Sequence ID No:2, Sequence ID No: 4, Sequence ID No: 133, Sequence ID No: 135 and Sequence ID No: 137.

29. A nucleotide sequence of claim 28, wherein said sequence is selected from the group of nucleotide sequences which code for the following protein fragments of Sequence ID No:2 consisting of amino acid residues 27-44, 46-48, 50-60, 66-67, 107-111, 120-121, 125-126, 155-160, 185-189, 214-223, 220-230, 240-245, 267-269, 273-282, 300-370 and 400-420.

30. A polypeptide of at least 6 amino acid residues selected from at least 6 consecutive amino acid residues of Seq. ID No: 2.

31. A polypeptide of at least 6 amino acid residues selected from at least 6 consecutive amino acid residues of Seq. ID No: 135.
32. A polypeptide having antigenic properties and selected from the group consisting of amino acid residues 27-44, 46-48, 50-60, 66-67, 107-111, 120-121, 125-126, 155-160, 185-189, 214-223, 220-230, 240-245, 267-269, 273-282, 300-370 and 400-420 of Sequence ID No: 2.
33. An antibody capable of specific binding to ARMP.
34. An antibody capable of specific binding to an ARMP extracellular domain.
35. An antibody capable of binding to a polypeptide in accordance with claim 29.
36. A bioassay for determining if a subject has a normal or mutant Alzheimer's related membrane protein (ARMP), said bioassay comprising:
- i) providing a biological sample of said subject;
  - ii) conducting a biological assay on said sample to detect a normal or mutant gene sequence coding for ARMP, a normal or mutant ARMP amino acid sequence or a normal or defective protein function.
37. A bioassay of claim 36, wherein said bioassay is a DNA or RNA based biological assay.
38. A bioassay of claim 37, wherein said biological assay is selected from the group consisting of probe hybridization, direct DNA sequencing, restriction enzyme analysis, electrophoretic mobility, RNase detection, chemical cleavage, ligase-mediated detection and PCR amplification.

39. A bioassay of claim 38, wherein said biological assay detects at least one mutation selected from the group consisting of :

- i) 685, A→C      ii) 737, A→G      iii) 986, C→A
- iv) 1105, C→G      v) 1478, G→A      vi) 1027, C→T
- vii) 1102, C→T      and      viii) 1422, C→G.

40. A bioassay of claim 36, wherein said bioassay is amino acid based biological assay.

41. A bioassay of claim 40, wherein said biological assay is selected from the group consisting of immunoassay, enzyme site specific assay, electrophoretic mobility of cleaved polypeptides.

42. A bioassay of claim 41, wherein said selected biological assay detects at least one mutation selected from the group consisting of:

- i) M 146L;      ii) H 163R;      iii) A 246E;
- iv) L 286V;      v) C 410Y;      vi) A 260V;
- vii) A 285V; and      viii) L 392V.

43. A bioassay of claim 36, wherein said biological assay detects normal or defective protein function.

44. A process for recombinantly producing Alzheimer's related membrane protein (ARMP) comprising culturing a host cell of claim 19 under suitable conditions to produce said ARMP by expressing said DNA sequence.

45. A therapeutic composition comprising Alzheimer's related membrane protein and a pharmaceutically acceptable carrier.

46. A recombinant vector for transforming mammalian tissue cells to express a therapeutically effective amount of Alzheimer's related membrane

protein in cells, said vector being delivered to cells by a suitable vehicle.

47. A recombinant vector of claim 46, wherein said tissue cells comprise liver, kidney, spleen, bone marrow and neurological cells.

48. A recombinant vector of claim 46, wherein said neurological cells comprise central nervous system cells of neuron, brain and vascular cell type.

49. A recombinant vector of claim 46 wherein said vehicle is selected from the group consisting of vaccinia virus, adenovirus, retrovirus, liposome transport, neurotropic viruses and Herpes simplex.

50. A method of treating a patient deficient in normal Alzheimer's related membrane protein (ARMP) comprising the step of administering to said patient a therapeutically effective amount of said protein targeted at a variety of patient cells which normally express ARMP.

51. A method of claim 50, wherein said variety of patient cells comprise heart, brain, lung, liver, skeletal muscle, kidney, pancreas and neurological cells.

52. An immunotherapy for treating a patient having Alzheimer's Disease due to cellular production of mutant ARMP, said immunotherapy comprising treating said patient with antibodies specific to said mutant ARMP, said antibodies binding mutant ARMP to reduce thereby levels of mutant ARMP in said patient.

53. An immunotherapy of claim 52, wherein said antibodies are developed by said patient's immune system upon administration to said patient of a vaccine comprising said mutant ARMP and a pharmaceutically acceptable carrier.



54. A vaccine composition for invoking an immune response in a human susceptible to Alzheimer's Disease, said composition comprising a mutant ARMP and a pharmaceutically acceptable carrier.

55. A method of treating a patient of Alzheimer's Disease comprising administering to said patient a therapeutically effective amount of a ligand or chemical molecule which corrects symptoms associated with expression of mutant ARMP gene.

56. A transgenic animal model for animal symptoms of Alzheimer's disease, said animal model having within its genome a DNA molecule in accordance with claim 1 with at least one mutation which when expressed results in the presence or absence of mutant ARMP in the animal's cells and thereby manifests the symptoms.

57. A transgenic animal model of claim 56, wherein said mutation is at least one nucleotide mutation.

58. A transgenic animal model of claim 56, wherein said polynucleotide sequence is Sequence ID No: 1.

59. A transgenic animal model of claim 56, wherein said polynucleotide sequence is Sequence ID No: 3.

60. A transgenic animal of claim 58, wherein said sequence mutations are selected from the group consisting of:

- i) 685, A→C      ii) 737, A→G      iii) 986, C→A
- iv) 1105, C→G      v) 1478, G→A      vi) 1027, C→T
- vii) 1102, C→T      and      viii) 1422, C→G.

61. A transgenic animal of claim 58, wherein said animal is a rodent.

62. A transgenic animal of claim 58, wherein said animal is a mouse.

63. A transgenic mouse model for Alzheimer's disease, said mouse having said mammalian polynucleotide of claim 134 with a mutation which when expressed results in the presence or absence of a mutant ARMP in the animal's cells and thereby manifest the syndrome.

64. A transgenic mouse exhibiting a physiological or neurological disorder which can be linked to one more mutations in the mouse ARMP gene or mouse ARMP.

65. A transgenic mouse of claim 64 exhibiting symptoms of cognitive, memory or behavioural disturbances.

66. A transgenic mouse of claim 65 exhibiting tissue cell disorders in heart, brain, lung, liver, skeletal muscle, kidney, pancreas and neurological cells.

67. Use of a transgenic animal of claim 56 for screening proteins, ligands and chemical molecules for efficacy in reversing effects of Alzheimer's Disease.

68. Use of a transgenic mouse of claim 63 for screening proteins, ligands and chemical molecules for efficacy in reversing effects of Alzheimer's Disease.

69. An isolated DNA molecule comprising a nucleotide sequence coding for a mutant form of E5-1 protein.

70. The DNA molecule of claim 69 wherein the nucleotide sequence has at least one mutation selected from the group consisting of:

- i) 787, A→T and
- ii) 1080, A→G.

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71. Substantially pure mutant E5-1 protein.

72. The protein of claim 71 having a mutation selected from the group consisting of:

- i) Asn141Ile and
- ii) Met239Val.

Add B3

Add C5

Add D2

Add F1